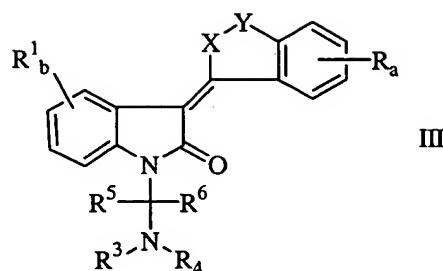
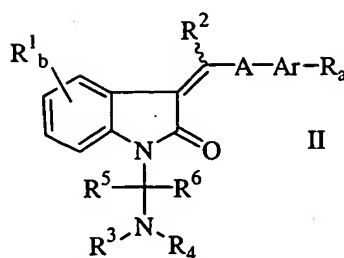


CLAIMS

What Is Claimed Is:

1. A compound represented by the general formula II or III:



wherein;

X is O or $C(R^2)_2$;

Y is $[C(R^2)_2]_c$;

A is absent;

R^1 is independently selected from the group consisting of halogen, hydroxy, nitro, cyano, hydrocarbyl and substituted hydrocarbyl radicals, wherein said substituted hydrocarbyl may be substituted with heteroatoms selected from the group consisting of halogen, nitrogen, phosphorus, sulfur and oxygen;

R^2 is selected from the group consisting of hydrogen, C_1 to C_8 alkyl, $(CR^8R^9)_dC(O)OR^{10}$, $COCH_3$, CH_2CH_2OH , $CH_2CH_2CH_2OH$ and phenyl;

R is selected from the group consisting of halogen, hydrocarbyl and substituted hydrocarbyl radicals, wherein said substituted hydrocarbyl may be substituted with heteroatoms selected from the group consisting of halogen, nitrogen, phosphorus, sulfur and oxygen;

R^3 and R^4 are independently selected from the group consisting of hydrogen, hydrocarbyl and substituted hydrocarbyl radicals, wherein said substituted hydrocarbyl may be substituted with heteroatoms selected from the group

consisting of halogen, nitrogen, phosphorus, sulfur and oxygen, or R^3 and R^4 , together with the nitrogen atom may form a cyclic ring, which ring may be substituted with said heteroatoms;

R^5 and R^6 are independently selected from the group consisting of hydrogen, alkyl and aryl radicals; provided that said alkyl or phenyl radicals may be substituted with from one to three halo, hydroxyl, lower alkyloxy or lower alkyl amino radicals;

R^{10} is hydrogen, C_1 to C_8 alkyl or arylalkyl;

a is 0 or an integer of from 1 to 3;

b is 0 or an integer of from 1 to 3;

c is an integer of from 1 to 2;

d is 0 or an integer of from 1 to 5

e is an integer of from 2 to 5

the wavy line represents a E or Z bond and Ar is selected from the group consisting of aryl, substituted aryl, heteroaryl, and substituted heteroaryl, wherein said substituted aryl or heteroaryl may be substituted with heteroatoms selected from the group consisting of halogen, nitrogen, phosphorus, sulfur and oxygen.

2. The compound of claim 1 wherein R is selected from the group consisting of halogen, C_1 to C_8 alkyl, CF_3 , OCF_3 , OCF_2H , CH_2CN , CN , SR^2 , $(CR^8R^9)_dC(O)OR^2$, $(CR^8R^9)_dC(O)N(R^2)_2$, $(CR^8R^9)_dOR^2$, $HNC(O)R^2$, $HN-C(O)OR^2$, $(CR^8R^9)_6N(R^2)_2$, $SO_2(CR^8R^9)_dN(R^2)_2$, $OP(O)(OR^2)_2$, $OC(O)OR^2$, OCH_2O , $HN-CH=CH$, $-N(COR^2)CH_2CH_2$, $HC=N-NH$, $N=CH-S$, $O(CR^8R^9)_eR^7$, $(CR^8R^9)_dR^7$, $-NR_2(CR^8R^9)_eR^7$ wherein R^7 is selected from the group consisting of halogen, 3-fluoropyrrolidinyl, 3-fluoropiperidinyl, 2-pyridinyl, 3-pyridinyl, 4-pyridinyl, 3-pyrrolinyl, pyrrolidinyl, piperidinyl, methyl isonipecotate, N-(2-methoxyethyl)-N-methylamyl, 1,2,3,6-tetrahydropyridinyl, morpholinyl, hexamethyleneiminyl, piperazinyl-2-one, piperazinyl, N-(2-methoxyethyl)ethylaminyl, thiomorpholinyl, heptamethyleneiminyl, 1-piperazinylcarboxaldehyde, 2,3,6,7-tetrahydro-(1H)-1,4-diazepinyl-5(4H)-one, N-

methylhomopiperazinyl, (3-dimethylamino)pyrrolidinyl, N-(2-methoxyethyl)-N-propylaminyl, isoindolinyl, nipecotamidinyl, isonipecotamidinyl, 1-acetylpiperazinyl, 3-acetamidopyrrolidinyl, trans-decahydroisoquinolinyl, cis-decahydroisoquinolinyl, N-acetylhomopiperazinyl, 3-(diethylamino)pyrrolidinyl, 1,4-dioxo-8-azaspiro[4.5]decaninyl, 1-(2-methoxyethyl)-piperazinyl, 2-pyrrolidin-3-ylpyridinyl, 4-pyrrolidin-3-ylpyridinyl, 3-(methylsulfonyl)pyrrolidinyl, 3-picolylmethylaminyl, 2-(2-methylaminoethyl)pyridinyl, 1-(2-pyrimidyl)-piperazinyl, 1-(2-pyrazinyl)-piperazinyl, 2-methylaminomethyl-1,3-dioxolane, 2-(N-methyl-2-aminoethyl)-1,3-dioxolane, 3-(N-acetyl-N-methylamino)pyrrolidinyl, 2-methoxyethylaminyl, tetrahydrofurfurylaminy, 4-aminotetrahydropyran, 2-amino-1-methoxybutane, 2-methoxyisopropylaminyl, 1-(3-aminopropyl)imidazole, histamyl, N,N-diisopropylethylenediaminyl, 1-benzyl-3-aminopyrrolidyl 2-(aminomethyl)-5-methylpyrazinyl, 2,2-dimethyl-1,3-dioxolane-4-methanaminyl, (R)-3-amino-1-N-BOC-pyrrolidinyl, 4-amino-1,2,2,6,6-pentamethylpiperidinyl, 4-aminomethyltetrahydropyran, ethanolamine and alkyl-substituted derivatives thereof; provided said alkyl or phenyl radicals may be substituted with one or two halo, hydroxy or lower alkyl amino radicals; wherein R⁸ and R⁹ may be selected from the group consisting of H, halogen, hydroxy, and C₁-C₄ alkyl or CR⁸R⁹ may represent a carbocyclic ring of from 3 to 6 carbons.

3. The compound of claim 2 wherein R⁵ and R⁶ are hydrogen.
4. The compound of claim 3 wherein R³ and R⁴, together with the nitrogen atom, form a 5 or 6 member ring.
5. The compound of claim 4 wherein R³ and R⁴, together with the nitrogen atom, form a ring selected from the group consisting of morpholinyl or piperidinyl.

6. The compound of claim 3 wherein R^3 is H and R^4 is selected from the group consisting of alkyl or alkyloxyalkyl.

7. The compound of claim 3 wherein R^1 is selected from the group consisting of halogen, C_1 to C_8 alkyl, phenyl, CF_3 , OCF_3 , OCF_2H , CN , SR^2 , $(CH_2)_dC(O)OR^2$, $C(O)N(R^2)_2$, $(CH_2)_dOR^2$, $HNC(O)R^2$, $HN-C(O)OR^2$, $(CH_2)_dN(R^2)_2$, $SO_2N(R^2)_2$, $OP(O)(OR^2)_2$, $OC(O)OR^2$, OCH_2O , $HN-CH=CH$, $-N(COR^2)CH_2CH_2HC=N-NH$, $N=CH-S$, $O(CH_2)_d-R^7$ and $(CH_2)_c-R^7$ wherein R^7 is selected from the group consisting of pyrrolidinyl, piperidinyl, pyrazinyl and morpholinyl and lower alkyl-substituted derivatives thereof; provided that R^7 and/or said alkyl or phenyl radicals may be substituted with from one to three, halo, hydroxyl, lower alkyloxy or lower alkyl amino radicals.

8. The compound of claim 3 wherein Ar is selected from the group consisting of phenyl, naphthyl, pyridyl, pyrrolyl, furyl, thienyl and substituted derivatives thereof.

9. The compound of claim 8 wherein Ar is phenyl or pyrrolyl.

10. The compound of claim 3 wherein said compound is represented by formula II.

11. The compound of claim 10 wherein Ar is pyrrolyl.

12. The compound of claim 11 wherein a and b are 0.

13. The compound of claim 11 wherein a is 2 and R is methyl.

14. The compound of claim 11 wherein b is 1 and R^1 is chloro.

15. The compound of claim 3 wherein said compound is represented by formula III.

16. The compound of claim 15 wherein X is O and Y is CH₂.

17. The compound of claim 16 wherein a and b are 0.

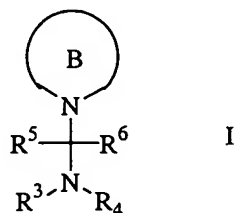
18. The compound of claim 16 wherein a is 1 and R is dimethylamino.

19. The compound of claim 3 selected from the group consisting of

3-(5-Dimethylamino-3H-isobenzofuran-1-ylidene)-1-piperidin-1-ylmethyl-1,3-dihydro-indol-2-one and

5-Chloro-3-(5-dimethylamino-3H-isobenzofuran-1-ylidene)-1-piperidin-1-ylmethyl-1,3-dihydro-indol-2-one

20. A compound represented by the general formula I:



wherein fragment B represents a tyrosine kinase inhibitor or serine threonine kinase inhibitor containing a nitrogen atom capable of reacting with formaldehyde, a substituted aldehyde or substituted ketone and an amine to provide a compound of formula I and R³ and R⁴ are independently selected from the group consisting of hydrogen, hydrocarbyl and substituted hydrocarbyl radicals, wherein said

substituted hydrocarbyl may be substituted with heteroatoms selected from the group consisting of halogen, nitrogen, phosphorus, sulfur and oxygen, or R^3 and R^4 , together with the nitrogen atom may form a cyclic ring, which ring may be substituted with said heteroatoms; and R^5 and R^6 are independently selected from the group consisting of hydrogen, alkyl and aryl radicals; provided said alkyl or phenyl radicals may be substituted with one to three halo, hydroxyl, lower alkyloxy or lower alkyl amino radicals and further provided said compound is not

1-Piperidin-1-ylmethyl-3-(1-H-pyrrol-2-ylmethylene)-1,3-dihydro-indol-2-one,

1-Morpholin-4-ylmethyl-3-(1H-pyrrol-2-ylmethylene)-1,3-dihydro-indol-2-one,

1-(4-Methyl-piperazin-1-ylmethyl)-3-(1H-pyrrol-2-ylmethylene)-1,3-dihydro-indol-2-one,

1-[(3-Methoxy-propylamino)-methyl]-3-(1H-pyrrol-2-ylmethylene)-1,3-dihydro-indol-2-one,

1-Butylaminomethyl-3-(1H-pyrrol-2-ylmethylene)-1,3-dihydro-indol-2-one,

5-Chloro-3-(3,5-dimethyl-1H-pyrrol-2-ylmethylene)-1-piperidin-1-ylmethyl-1,3-dihydro-indol-2-one,

5-Chloro-3-(3,5-dimethyl-1H-pyrrol-2-ylmethylene)-1-morpholin-4-ylmethyl-1,3-dihydro-indol-2-one,

3-(3H-Isobenzofuran-1-ylidene)-1-piperidin-1-ylmethyl-1,3-dihydro-indol-2-one or

3-(3H-Isobenzofuran-1-ylidene)-1-morpholin-4-ylmethyl-1,3-dihydro-indol-2-one.

21. A method for treating diseases related to unregulated tyrosine kinase signal transduction, the method comprising the step of administering to a subject in need thereof a therapeutically effective amount of a compound according to claim 1.
22. The method of claim 21 wherein said disease is selected from the group consisting of cancer, blood vessel proliferative disorders, fibrotic disorders, mesangial cell proliferative disorders and metabolic diseases.
23. The method of claim 21 wherein the blood vessel proliferative disorder is selected from the group consisting of diabetic retinopathy, age-related macular degeneration, retinopathy of prematurity, arthritis and restenosis.
24. The method of claim 21 wherein the fibrotic disorder is selected from the group consisting of hepatic cirrhosis, atherosclerosis and surgical adhesions.
25. The method of claim 21 wherein the mesangial cell proliferative disorder is selected from the group consisting of glomerulonephritis, diabetic nephropathy, malignant nephrosclerosis, thrombotic microangiopathy syndromes, transplant rejection and glomerulopathies.
26. The method of claim 21 wherein the metabolic disorder is selected from the group consisting of psoriasis, diabetes mellitus, wound healing, inflammation and neurodegenerative diseases.